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Case Report Open Access

# Report of Initial Experience with a Novel Extracellular Matrix Material Derived from Porcine Urinary Bladder to Treat Patients with Vesico-Vaginal Fistula

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## Abstract

Our objective was to report our initial experience with extracellular matrix material derived from porcine urinary bladder, MatriStem, in patients with vesico vaginal fistula (VVF).

**Materials and methods:** For our retrospective review, we obtained the medical records of 40 consecutive patients who were seen for VVF during our 2 years study period. All patients underwent a thorough evaluation, including history, physical, examination, computed tomography urography, and single-dye pad tests. The cases were treated with two different kinds of MatriStem to repair VVF.

**Results:** In 6 patients, the MatriStem procedure was performed by robotic surgery, in these cases a MatriStem graft were used; in 3 cases we injected micronized particles of MatriStem via cystoscopy and vaginoscopy. The mean follow-up 7.25 months. We observed that 75% of the cases had no fistula drainage per the vagina and progressed to full healing.

**Conclusion:** MatriStem in our early results seem to have a role in effectively treating VVF. Further investigation and long term follow up is needed to establish MatriStem as An alternative treatment for VVF patients.

**Keywords:** Vesico-vaginal fistula; Urinary bladder fistula; Urinary bladder matrix

## Introduction

A vesicovaginal fistula (VVF) is an abnormal, pathologic communication between the bladder and vagina, resulting in continuous urinary incontinence. In developing countries, where access to prenatal and obstetric care is limited, women most commonly develop a VVF from ischemia and pressure necrosis in the vaginal wall during prolonged or obstructed delivery labor. In developed countries, the most common cause of a VVF is a cystotomy during pelvic surgery, most often during a hysterectomy. Vesicovaginal fistulas occur uncommonly and depending on the fistula size, urinary incontinence can be significant; however, even small fistulas burden affected women, physical, psychological and socially [1-4].

The true incidence of vesicovaginal fistulas is unknown but it has been estimated at 0.3% to 2% [5]. With advances in obstetrical care the majority of vesicovaginal fistulas in developed countries develop after gynecologic surgery with abdominal hysterectomy causing approximately 90%. Other causes of a vesicovaginal fistula include anti-incontinence procedures (bladder neck suspension and anterior colporrhaphy), radiation, malignancy, infection, trauma and a foreign body [5].

Management of VVFs ranges from conservative measures including prolonged bladder drainage to more invasive therapies such as endoscopic, laparoscopic or open repair as well as vaginal surgery approach to repair VVF. Many urologists favour transvesical operations because they are experienced with this approach. The transperitoneal approach offers an opportunity for wide exploration and the use of a peritoneal or omental graft in managing larger fistulae [6,7]. If there is associated intra-abdominal pathology, the abdominal approach allows concomitant procedures. However, some authors describing larger series of patients report the exclusive use of the vaginal approach [7].

The best chance of a successful repair is at the first attempt. The method of closure depends on the surgeon's training and experience. Although simple fistula can be closed by either approach, the vaginal is easier, safer and more comfortable. Adjuvant techniques are needed for complex fistula[7]. The principles of vesicovaginal fistula repair include: (1) adequate exposure of the fistula tract; (2) a watertight closure; (3) well-vascularized tissue used for the repair; (4) multiple layer closure; (5) tension-free, non-overlapping suture lines; (6) adequate urinary drainage early after the repair [7].

The quality of the tissue to repair the VVF has a role, improving this tissue condition increases the possibility of closing the VVF by surgery repair. MatriStem, a sterile extracellular matrix product (ACell Corporation, Columbia, MD), was designed to promote wound healing and tissue repair. Derived from porcine urinary bladder, it contains numerous growth factors, collagens, an intact epithelial basement membrane, and antimicrobial factors as well as to provides a biomechanical scaffold to aid in growth of native tissues [3,4]. Porcine-derived urinary bladder matrix (UBM) has been used clinically to treat patients with chronic wounds [1,2].

Our objective was to report our initial experience with extracellular matrix material derived from porcine urinary bladder, MatriStem, in patients with VVF.

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## Materials and Methods

For our retrospective review, we obtained the medical records of 40 consecutive patients who were seen for VVF during our 2 years study period (January 2013 through December 2014) in the urology clinic at the University of Minnesota medical center. Clinical variables (age, body mass index and comorbidities); VVF causes and locations; numbers and types of procedures performed such as open, endoscopy or robotic surgery, their surgical outcomes, complications, time of using urinary catheter and follow-up were assessed and reported for the review. No control group is presented in this study due to this is a retrospective chart review about the outcomes for procedure performed with a new novel material, MatriStem**.**

Before the UBM procedure, all patients underwent a thorough evaluation, including history, physical examination, computed tomography (CT) urography, and single-dye pad tests. The cases were treated with two different kinds of MatriStem to repair VVF. Some of them were treated with a micronized particles (1000 mg) of UBM reconstituted of saline solution and other were treated with a grafts 5 × 5 cm sheets which ones were rehydrated for 10 minutes in room temperature in a sterile saline solution. All patients were evaluated with urethro-cystography before taking out the urinary catheter.

## Results

Clinical characteristics, comorbidities, etiologies and surgical procedures are summarized in Tables 1 and 2. Of the 40 VVF patients, 8 were treated with MatriStem (mean age, 48.25 years; mean body mass index, 28.6). Before the UBM procedure, all patients had symptoms and CT images (Figure 1A and 1B) consistent with a VVF. Comorbidities included type 2 Diabetes mellitus (n=1), endometrial cancer (n=1), and rectal cancer (n=1). The most common previous surgery was hysterectomy (n=4); in addition, 2 patients had undergone pelvic radiation, and 4 cases had undergone 1 or more attempts to repair their VVF before the MatriStem procedure. VVF causes were hysterectomy (n=4), proctectomy (n=1), pelvic organ prolapse repair or other pelvic surgery (n=2), and C–section with bladder injury (n=1). The mean VVF duration before the MatriStem procedure was 51 weeks. In 7 patients, the VVF location was in the posterior bladder behind the trigone.

| Matristem Treatment | | |
|---|---|---|
| | N | 8 |
| | Mean Age | 48.25 |
| | Mean BMI | 28.6 |
| Comorbidities | | |
| | Diabetes mellitus | 1 |
| | Endometrial Cancer | 1 |
| | Rectal Cancer | 1 |
| Etiology | | |
| | Hysterectomy/C-Section | 4 |
| | Intra-abdominal Pelvic surgery | 2 |
| | Pelvic Radiation | 2 |
| | Pelvic Organ Prolapse repair | 1 |

**Table 1:** Clinical characteristics, comorbidities and etiologies of patients with vesico-vaginal fistulas treated by extracellular matrix material derived from porcine urinary bladder (MatriStem ACell).

| Type of procedure performed in patients with vesico-vaginal fistula | |
|---|---|
| Robotic Repair with ACell Interposition | N=5 |
| Endoscopic Injection<br>Vaginoscopy/cystoscopy<br>Micronized particle injection | N=4 |
| Transvaginal repair | N=2 |
| Combined Transvaginal and Injection | N=2 |
| Total | 13 |
| Number of Procedures per patient | |
| 3 | N=1 |
| 2 | N=2 |
| 1 | N=5 |
| Total | 8 |
| Mean/Median | 1.6/1 |

**Table 2:** Characteristics of surgical procedures of patients with vesico-vaginal fistulas treated by extracellular matrix material derived from porcine urinary bladder (MatriStem ACell).

In 6 patients, the MatriStem procedure was performed by robotic surgery, in these cases a MatriStem graft were used; in 3 cases we injected micronized particles of MatriStem via cystoscopy and vaginoscopy. The mean number of MatriStem graft placement attempts was 1.63; the mean duration of the procedure was 194.87 minutes. We noted no major complications during and after the procedure.

The mean follow-up 7.25 months. The mean duration of urinary catheter use was 6.3 weeks. We observed that 75% of the cases had no fistula drainage per the vagina and progressed to full healing. The single-dye pad tests and postoperative cystography including post-void phase imaging were negative in all these patients (Figure 2A and 2B). 3 patients required more than 1 procedure, 2 of them had pelvic radiation in their medical history. 2 Patients had a residual VVF after MatriStem procedure, both cases had pelvic radiation.

## Discussion

MatriStem is a commercially available porcine-derived a cellular UBM that is manufactured either in sheets or in the form of micronized

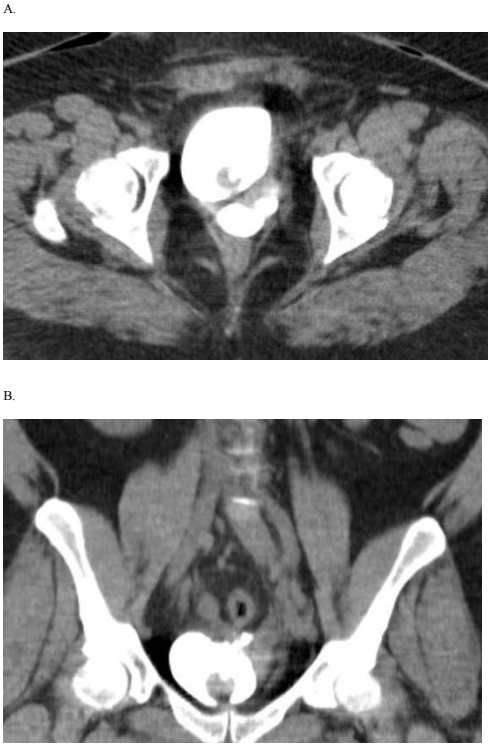


**Figure 1:** CT urography images of a vesicovaginal fistula in Patient 1. A – axial delayed-phase contrast enhanced image. B – coronal delayed-phase contrast- enhanced image.

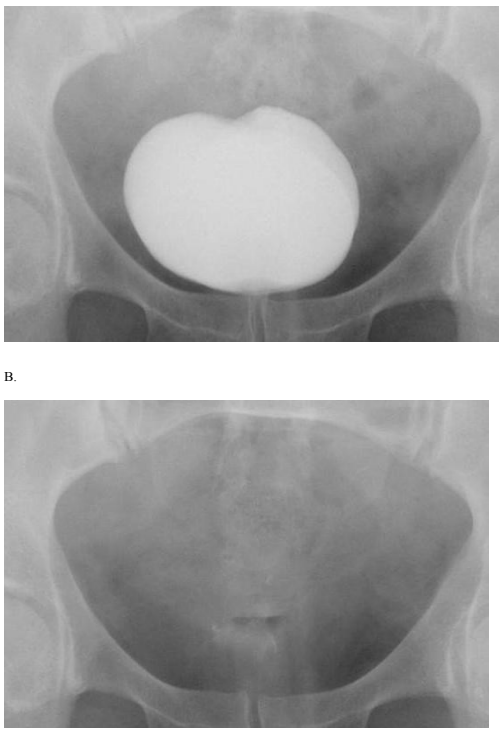


**Figure 2:** Cystography images 3 weeks after cystoscopic injection of urinary bladder matrix in Patient 1. A – image showing 300 mL contrast in bladder. B – post-void image showing no residual contrast or fistula.

particles termed MicroMatrix and effectively treats patients with VVF. In 2005, in the United States alone, more than 573,000 hysterectomies were performed [6]. The VVF incidence is estimated to be as high as 2% after a hysterectomy; clearly, then, it is not an uncommon problem [5]. Prolonged bladder drainage with an indwelling urethral catheter is an appealing first-line treatment; however, only 10% of women with a VVF < 3 mm will experience spontaneous fistula closure after 2 to 8 weeks [7]. Stovsky et al. theorized that electrofulguration of the fistula epithelial lining may lead to fibrosis, scarring, and closure of the tract. Yet early series found, at best, a 58% success rate with fulguration as the primary therapy for women with small (< 3.5 mm) iatrogenic VVFs [8].

The development of new tissue adhesives and hemostatic agents has ushered in alternative therapies for women with VVFs. Muto et al. found that cyanoacrylic glue injected vaginally into the fistula tract cured 2 of 3 patients with moderate-size (7 to 15 mm) VVFs [9-15]. Shirvan et al. evaluated platelet-rich plasma and fibrin glue in 12 VVF patients, with an overall success rate of 91%. Despite that encouraging 91% success rate, the preparation of platelet-rich plasma and fibrin glue is labor-intensive, and the patients required postoperative bed rest for 3 days to allow for clot maturation [16].

Surgical repair remains the mainstay for treating VVFs. Early successful repairs involved excision of the fistulous tract, but the risks included increased blood loss and conversion to a larger fistula. Nowadays, the gold standard is the O'Connor technique: its adoption for supratrigonal fistulas has resulted in excellent outcomes, with a success rate of greater than 90% when paired with an interposition flap [9-11]. Laparoscopy, and more recently robot-assisted surgery, have enabled the minimally invasive application of the O'Connor technique; outcomes, as compared with open procedures, are comparable - with improvements in pain control, in hospital length of stay, in cosmesis, and in return to baseline function [12-14].

The transvaginal approach to VVF repair is also highly successful, particularly when performed with a peritoneal or Martius flap. Using a transvaginal approach in a large retrospective series, Eilber et al. achieved a 96% fistula closure rate. Use of a peritoneal flap greatly improves the success of open repair, including salvage procedures [5]. Despite the success of the transvaginal approach, it is associated with an increased surgical risk and morbidity.

MatriStem is a resorbable, acellular material from the lamina propria of porcine urinary bladder, UBM is decellularized, lyophilized, and sterilized. When implanted, it stimulates neovascularization through a number of growth factors and functional proteins such as collagen, laminin, and elastin [2]. A comprehensive protein expression profile of UBM demonstrated 129 proteins, with 19% of them playing a role in cell structure, 13% in cellular adhesion, and 1% in promotion of tissue remodeling [3]. UBM has safely been used in various settings to promote wound healing, including in patients with chronic non-healing ischemic and radiation-induced cutaneous wounds [1,2]. Inflammatory reactions are uncommon, given the acellular, inert nature of UBM [4].

In our study, we reported that 6 cases reached a complete healing of the VVF. 2 cases had a radiation history. Also in new data that have not been reported, with a longer follow-up (1.5 years), there is no recurrence on those cases. This material has been reported to be useful in radiation-induced cutaneous wounds. More complex VVF in these both cases could explain that the procedure were not enough to reach a complete healing. MatriStem would be useful to treat patient with VVF. No control group was presented in this retrospective report about a procedure with MatriStem. However, this it could be an opportunity for futures protocols to compare a VVF repair with MatriStem versus repair with the standard procedures currently performed; further investigation is needed to establish MatriStem as a standard treatment for VVF patients.

## Conclusion

MatriStem in our early results seem to have a role in effectively treating VVF. Further investigation and long term follow up is needed to establish MatriStem as An alternative treatment for VVF patients.

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